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Assessment of Sleep Pattern in Egyptian Elderly Subjects with Vascular Dementia: An Egyptian Study on Elderly Population

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Abstract

Background: Sleep is considered to be very important for cognitive function and also cognitive deficits and sleep disorders are influenced by one another. Currently, growing evidence suggests that sleep disturbances is common in vascular dementia (VaD).

Study Objectives: The goal of the current study was to assess the disturbance in sleep pattern in patients with vascular dementia (VaD) and compare it to healthy normally cognitive elderly individuals. The study further investigated whether meaningful differences in the Subjective sleep assessment (ESS and PSQI) and sleep measurements (PSG) in VaD patients.

Study Design/Method: Overnight PSG recordings and self-reported sleep measures were obtained from 20 healthy elderly subjects and 20 VaD patients at the sleep laboratory.

Results: This study showed abnormal subjective sleep quality in all patients and revealed that the most common sleep complaints among VaD patients were excessive daytime sleepiness (EDS), sleep disordered breathing (SDB), insomnia and RLS and PLMS and REM behavioral disordered, respectively. Moreover, patients spent more time in stage I sleep, but less time in SWS and REM sleep compared to control populations, with delayed REML and less 1st REML. In addition, increased sleep fragmentation (WASO and SFI) and increased AI and PLMS index were detected in VaD patients. Finally, VaD patients had significantly ($p < 0.05$) high apnea, hypopnea and RDI score with high average SpO_2 desaturation.

Conclusions: It is conclude that sleep is significantly ($p < 0.05$) impaired in patients with VaD at both the objective and subjective levels which may be used as a diagnostic marker of VaD. SBD is a common feature of VaD leading to fragmented sleep, increased nocturnal confusion and excessive daytime sleepiness. Subjective sleep assessment questionnaire by (ESS and PSQI) can be used in VaD patients when objective sleep assessment by PSG recordings is difficult to be done. The PSG study of sleep continuity, sleep architecture and REM sleep may help in the prevention of progression of VaD.

Keywords: *REM and NREM Sleep Disturbances; Vascular Dementia; Subjective Sleep Assessment; Polysomnography*

Introduction

Vascular dementia (VaD), the second most common cause of dementia after AD, represents not less than 20% of cases and is expected to increase in coming years [1]. The pervasiveness of both VaD and AD rises dynamically with age, with the risk of VaD doubling every 5.3 years [2]. Vascular-type pathology and mixed pathology are respectively two and three times more likely in demented patients [3]. Be-

cause of their dependency and negative financial impact upon their families and healthcare providers, VaD is a major public health issue and its prevention is of paramount importance considering the reduced quality of life for the patients [4].

Sleep is important to normal cognitive functioning, particularly for the formation and consolidation of new memories. Circadian rhythm and sleep complaints are common in the aging population, particularly in those with dementia [5]. In vascular dementia, neuropsychiatric manifestations are very common (90%) and the most common presenting symptoms are sleep disturbances (61%), depression (46%) and apathy (44%). Sleep disturbance is one of the most important domains of behavioral and psychological symptoms in patients with dementia reducing their quality of life. Past research has demonstrated that sleep disturbance is related to reduce executive function and an increased mortality rate in older adults [6].

Accurately diagnosing sleep disorders in dementia patients can be quite tricky, due to an abundance of underlying causes, mitigating factors and common causal symptoms. Given the rising prevalence of vascular dementia with aging, the development of more sensitive diagnostic and prognostic tools will be critical for elucidating and modifying VaD pathophysiology to alleviate the personal and socio-economic impact of cognitive decline in the elderly [7]. As if there is any delay of early detection or correct treatment, vascular cognitive impairment (VCI) may progress to dementia [8]. Also, patients with mixed pathologies have nearly twice the incremental risk of dementia compared with patients with only Alzheimer-type lesions. Consequently, many cases of dementia could either be prevented or delayed by targeting the vascular component [3].

Considering the adverse effect of Vad on sleep, this study was designed to assess the disturbance in sleep pattern both the subjective sleep assessment (ESS and PSQI) and objective sleep measurements (PSG) in patients with VaD comparing it with healthy cognitive elderly individuals.

Subject and Methods

Subjects

Twenty VaD patients (10 males and 10 females; mean age: 66.05 ± 2.04)) were recruited based on the criteria of Vascular Dementia in DSM-V [9]. Another 20 healthy subjects (10 males and 10 females with mean age: 65.25 ± 2.22y) were also enrolled in the study, after they signed an informed consent. Experimental procedures were previously approved by the Ethical Committee for Human Research at the Faculty of Medicine A in Shams University.

Both healthy subjects and VaD patients underwent full medical, neurological, psychiatric history and clinical examinations. Brain magnetic resonance imaging (MRI) was also performed on all candidates. Exclusion criteria included other types of dementias, psychiatric disorders affecting sleep, and/or major medical illness affecting sleep and the use of medication affecting the sleep-wake cycle. Patients were at mild to moderate stages of VaD, as assessed using the Clinical Dementia Rating (CDR) [10] and the Mini-Mental State Examination. Cognitive assessment included Mini Mental State Examination (MMSE) which was used to provide a simple global measure of cognitive functioning [11]. Mood assessment included Geriatric Depression Scale (GDS) which was used to identify depression in the elderly [12]. Cornell Scale for Depression in Dementia [13] and Taylor Anxiety Scale A were used to exclude patients with anxiety [14]. Subjective sleep assessment was assessed using psychometric sleep assessment questionnaire (applied to the care givers), an Arabic version for sleep evaluation [15]. This instrument included validated Arabic translations of other sleep assessment scales employing (A)- The Pittsburgh Sleep Quality Index (PSQI) [16] and (B)- the Subjective daytime sleepiness which was assessed using the Epworth Sleepiness Scale (ESS) [17]. Objective sleep assessment was assessed using PSG. PSG records included the following parameters:- the electroencephalogram (EEG, leads C3-A2 and 01-A2), electrooculogram (EOG), electromyogram of the chin (chin EMG) and the electrocardiogram (ECG)In addition, the abdominal and thoracic respiratory movements, oral and nasal airflows and arterial oxygen saturation were also measured to exclude sleep apnoea syndrome. The PSG recordings were taken from 22: 00 to 7: 00 of the following day. The PSG parameters were scored by visual assessment using the standard criteria [18].

The following data were analyzed:

(a) Sleep efficiency and continuity indices sleep latency (SL, the time span between "lights out" and onset of the first stage of sleep), sleep efficiency (SE, the percentages of the sleep time for the recording time) and arousal index (AI, a tendency for more wake after sleep onset arousal).

(b) Hypnogram indices: The percentage of stage I, II, III, IV and SWS sleep for total sleep time (Stage I, II, III, IV and SWS %) and the percentage of REM sleep for total sleep time (REM %).

(c) REM sleep indices, the following were analyzed: REM; duration of REM time in total sleep time, 1st REMD; first REM period duration and REML; REM latency (the time span between sleep onset and onset of the first REM sleep).

(d) Respiratory events includes APNEA/H, HYPONE/H, RDI (Respiratory Distress Index) and Oxygen Saturation (SPO_2) and finally

(e) PLMs; periodic limb movements.

Statistical analysis

Data were processed by standard analytical procedures [19] to determine the awake-time after sleep onset, sleep efficiency, percentage of non-REM sleep in Stages 1 to 3 of sleep, percentage of REM sleep, and REM sleep latency. The results are expressed as mean ±, standard deviation (SD) or number (percent). Comparison between categorical data [number (percent)] was performed using Chi square test. Comparison between values of different variables in the two studied groups was performed using either unpaired Student's t- test or Mann-Whitney test whenever it was appropriate. Correlation between sleep parameters and different parameters in patient group was performed using either Pearson or Spearman's Rank correlation coefficient. SPSS computer program (version 19 windows) was used for data analysis. P value ≤ 0.05 was considered significant.

Results

Demographic data

VaD patients and control group showed similar demographic profiles as shown in table 1. There were with no statistical significant difference as regards either age or sex between both groups. However, there was statistical significant difference ($p < 0.05$) between both groups regarding BMI with high BMI in the VaD group compared to control.

Demographic features	VaD group (n = 20)	Control (n = 20)	P value
Age (yrs.)			
Min.-maximum	62.0 - 69.0	61.0 - 69.0	
Mean ± SD	66.05 ± 2.04	65.25 ± 2.22	0.243
Sex			
Female	10 (50%)	10 (50%)	1.000
Male	10 (50%)	10 (50%)	
BMI			
Min.-maximum	19.7 - 26.8	19.5 - 25.0	
Mean ± SD	23.81 ± 2.32	22.29 ± 1.69	0.026*

Table 1: *Demographic features in the two studied groups (Data are mean ± SD; n = 20 for each group; *p < 0.05).*

In this study, the results also show that there was statistical significant difference ($p < 0.05$) between group VaD and control regarding hypertension and hyperlipidemia. Sleep disorders were present in 20 patients (100%) in VaD group, but only in 5 (25%) patients in control group. The sleep disorders were insomnia in 3 (15%) patients, excessive daytime sleepiness in 13 (65%) patients, sleep disordered breathing (SDB) in 10 (50%) patients, REM behavioral disordered in one (5%) patient and RLS and PLM in 3 (15%) patients.

As regards activities of Daily Living (ADL) there was statistical significant difference ($p < 0.05$) between group VaD and control with most of VaD patients had low ADL. There was statistical significant difference ($p < 0.05$) between VaD group with control group regarding CDR as shown in table 2.

CDR	VaD group (n = 20)	Control (n = 20)	P value
0	0 (0.0%)	20 (100.0%)	
1	5 (25.0%)	0 (0.0%)	0.001*
2	15 (75.0%)	0 (0.0%)	

Table 2: *Clinical dementia rating scale (CDR) in the two studied groups (Data expressed as a percentage; *p < 0.05).*

The results for MMSE are shown in table 3 revealing a statistical significant difference ($p < 0.05$) between VaD group with control group.

MMSE	VaD group (n = 20)	Control (n = 20)	P value
Normal	0 (0.0%)	20 (100.0%)	
Mild	5 (25.0%)	0 (0.0%)	0.001*
Moderate	15 (75.0%)	0 (0.0%)	

Table 3*: MMSE in the two studied groups (Data expressed as a percentage; n = 20; *p < 0.05.*

Regarding the MRI brain results VaD group, the data reveal large cortical infarctions in 10 (50%) patients, subcortical infarctions in 6 (30%) patients, lacunar infarcts in 9 (45%) patients, diffuse white matter hyper-intensities in 12 (60%) patients and brain atrophy in 20 (100%) patients**.**

Subjective sleep assessment

The results presented in table 4 show a statistical significant difference ($p < 0.001$) between VaD group compared with control group regarding ESS and PSQI with higher results among the patient group.

ESS	VaD group (n = 20)	Control (n = 20)	P value
0 - 5	0 (0.0%)	18 (90.0%)	0.001*
6 - 10	7 (35.0%)	2 (10.0%)	
11 - 12	5 (25.0%)	0 (0.0%)	
13 - 15	4 (20.0%)	0 (0.0%)	
16 - 24	4 (20.0%)	0 (0.0%)	
PSQI	**VaD group (n = 20)**	**Control (n = 20)**	**P value**
< 5	0 (0.0%)	20 (100.0%)	0.001*
> 5	20 (100.0%)	0 (0.0%)	

Table 4: *ESS and PSQI in the two studied groups (data expressed as percentages; n = 20; * p < 0.001).*

Table 5 shows Correlation between severity of the disease and subjective sleep assessment. The results show a statistical significant ($p < 0.007$) correlation between CDR and MMSE and PSQI (the severe cognitive impairment, the more the poor sleep quality). However, there

was no statistical significant correlation ($p > 0.05$) between CDR and MMSE and ESS (no relation between degree of cognitive impairment and excessive daytime sleepiness) (See table 5).

Sleep parameters	ESS		PSQ1	
	Correlation Coefficient	p value	Correlation Coefficient	p value
CDR	-0.187	0.430	0.579	0.007*
MMSE	-0.187	0.430	0.579	0.007*

***Table 5**: Correlation between severity of the disease and subjective sleep assessment; *p < 0.07).*

Polysomnography results

Table 6 show the polysomnography results in the two studied groups. Regarding sleep efficiency and continuity, the results showed poorer sleep efficiency, prolonged SL, and a tendency for more wake after sleep onset (AI) in patient group. With regards to hypnogram, the results showed that VaD patients spent more time in stage 1 and stage 2 sleep but had lower percentage of slow wave sleep (SWS) and REM sleep compared to control group. As regards REM parameters, the results showed VaD patients had lower percentage of REM sleep, delayed REML and decreased 1st REMD compared to control group. As regards Sleep fragmentation parameters, the data showed that VaD patients had short TST, more WASO (more time sent awake) and high SFI (more sleep stage shifts) compared to control group. Regarding respiratory event, VaD patients had more apnea, hypopnea, RDI and high SpO_2 desaturation compared to control group. Finally, regarding PLMs, there was a statistical significant ($p < 0.001$) increase of PLMs with RLS in VaD group in comparison to control groups (see table 5).

	VaD group (n = 20)	Control (n = 20)	P value #
SE	67.49 ± 18.69	88.10 ± 4.40	0.001**
SL	18.70 ± 13.22	18.60 ± 5.13	0.850
Arousal I	13.44 ± 12.27	1.66 ± 0.92	0.001**
I	47.96 ± 22.68	4.40 ± 1.13	0.001**
II	48.99 ± 22.01	50.22 ± 0.90	0.351
SWS	1.35 ± 4.80	21.52 ± 1.04	0.001**
REM	1.47 ± 2.45	23.80 ± 0.92	0.001**
REML	82.90 ± 92.87	65.10 ± 4.55	0.397
First REMD	1.65 ± 2.18	18.38 ± 0.30	0.001**
TST	166.49 ± 57.99	281.85 ± 36.95	0.001**
WASO	57.52 ± 33.87	16.12 ± 5.83	0.001**
SFI	0.51 ± 0.25	0.39 ± 0.09	0.046*
Apnea/H	15.51 ± 24.89	0.60 ± 0.81	0.173
Hypopnea/H	4.13 ± 6.33	0.22 ± 0.34	0.018*
RDI	21.62 ± 28.31	0.82 ± 1.10	0.013*
SPO_2	6.10 ± 12.70	0.12 ± 0.21	0.049*
PLMs	4.94 ± 8.26	1.15 ± 0.44	0.027*

***Table 6**: Polysomnography results in the two studied groups (Data are mean ± SD; n = 20; *p < 0.05 and **p < 0.001).*

Table 7 shows the correlation between sleep parameters in the patient group and ADL. Regarding sleep parameters in the VaD group in comparison to ADL scores, there were statistical significant ($p < 0.05$) negative correlation between AI and RDI and ADL and high AI and RDI was associated with low ADL (more functional impairment) but not for SE (see table 7).

Sleep parameters	ADL	
	Correlation Coefficient	p value
SE	-0.420	0.065
Arousal I	-0.541	0.014*
RDI	-0.791	0.001**

Table 7: *Correlation between Sleep parameters in the patient group and ADL; *p < 0.05 and **p < 0.001).*

Table 8 shows sleep parameters in the patient group classified according to BMI subgroups. The data reveal statistical significant ($p < 0.05$) difference for Apnea/H, RDI and SPO_2 and BMI score (more Apnea/H and RDI with high BMI index and more average SpO_2 desaturation with high BMI), but not for SE and AI.

	BMI < 25 (n = 13)	BMI > 25 (n = 7)	P value #
SE	67.21 ± 18.14	68.03 ± 21.16	0.968
Arousal I	12.02 ± 13.68	16.09 ± 9.49	0.143
Apnea/H	10.65 ± 28.64	24.54 ± 13.23	0.014*
RDI	14.77 ± 29.31	34.33 ± 23.00	0.047*
SPO_2	1.23 ± 2.42	15.14 ± 18.77	0.004*

Table 8: *Sleep parameters in the patient group classified according to BMI subgroups (Data are mean ± SD; n = 13 and 7; p < 0.05).*

Table 9 shows the correlation between sleep parameters and grade of dementia (MMSE and CDR) and PSQI in patient group. The results show no statistical significant difference ($p > 0.05$) regarding sleep parameters (SE, SL, SWS and AI) and grade of dementia (MMSE and CDR) and subjective sleep assessment (PSQI) in patient group.

	MMSE		CDR		PSQI	
	Pearson Correlation	p value	Spearman's Correlation	p value	Pearson Correlation	p value
SE	0.049	0.837	0.170	0.473	-0.030	0.901
SL	-0.115	0.628	-0.049	0.839	0.193	0.415
SWS	0.135	0.570	0.328	0.158	-0.227	0.336
Arousal index	0.147	0.536	-0.183	0.440	0.120	0.613

Table 9: *Correlation between sleep parameters and grades of dementia (MMSE and CDR) and PSQI in the patient group); *p > 0.05).*

Table 10 shows the correlation between sleep parameters and ESS score severity (normal, mild, moderate, severe. The data show statistical significant difference ($p < 0.05$) for SE, AI, Apnea/H, RDI and SPO_2 with the ESS score severity. Also, there was statistical significant ($p < 0.001$) difference for BMI in comparison to ESS score severity; severe ESS score with high BMI.

Sleep parameters	ESS	
	Correlation Coefficient	p value
SE	0.511	0.021*
Arousal I	0.578	0.008*
Apnea	0.900	0.001**
RDI	0.854	0.001**
SPO_2	0.810	0.001**
BMI	0.674	0.001**

***Table 10**: Correlation between sleep parameters and ESS score severity (normal, mild, moderate, severe); *p < 0.5 and **p < 0.001).*

Table 11 shows the correlation between sleep parameters and site of lesion while table 12 reveals correlation between sleep parameters and type of diffuse white matter hyper-intensities, degree of brain atrophy and side of the lesion. The data show no significant correlation (p > 0.05) between sleep parameters and MRI findings; either subjective sleep assessment; ESS and PSQI or objective PSG parameters; SE, SL, AI, RDI and SPO_2, WASO and SFI. The MRI findings include the presence of cortical or subcortical infarction, frontal, thalamic or lacunar infarction, different types of diffuse white matter hyper-intensities, degree of brain atrophy and side of infarction; left, right or bilateral (See tables 11 and 12).

	Large cortical infraction (n = 10)	Subcortical infraction (n = 6)	P value #
SE	67.68 ± 24.09	63.87 ± 12.35	0.550
SL	22.55 ± 15.95	24.33 ± 8.43	0.957
Arousal I	13.29 ± 15.66	12.73 ± 5.88	0.515
RDI	21.02 ± 33.50	9.30 ± 11.75	0.743
SPO2	7.10 ± 16.39	4.50 ± 11.02	0.428
WASO	53.15 ± 35.79	61.92 ± 38.17	0.664
SFI	0.43 ± 0.24	0.37 ± 0.12	0.703
PSQI	11.70 ± 2.16	10.83 ± 2.04	0.432
ESS	11.70 ± 3.20	11.67 ± 3.33	0.956
	Frontal (n = 6)	**Thalamic (n = 9)**	**P value**
SE	77.35 ± 19.17	65.03 ± 18.27	0.216
SL	16.83 ± 16.71	18.78 ± 14.20	0.679
Arousal I	18.53 ± 18.78	11.10 ± 9.63	0.443
SFI	0.51 ± 0.27	0.59 ± 0.27	0.516
SWS	0.43 ± 1.06	2.71 ± 7.08	0.674
REM	1.30 ± 1.77	0.89 ± 2.10	0.306
ESS	12.00 ± 3.95	11.78 ± 2.95	1.000
PSQI	12.17 ± 2.04	11.33 ± 1.73	0.369

***Table 11**: Correlation between sleep parameters and site of lesion (Data are mean ± SD; n = 10 and 6; p > 0.05).*

Sleep parameters	Type of diffuse white matter hyper-intensities	
	Correlation Coefficient	p value
SE	-0.023	0.944
SL	-0.291	0.359
Arousal I	0.496	0.101
RDI	0.321	0.310
SPO2	0.090	0.782
WASO	0.420	0.174
SFI	0.359	0.252
PSQI	-0.169	0.600
ESS	-0.043	0.895
BMI	0.460	0.132
Sleep parameters	**Degree of brain atrophy**	
	Correlation Coefficient	**p value**
SE	-0.288	0.219
SL	-0.174	0.462
Arousal I	0.392	0.087
RDI	0.236	0.316
SPO2	0.201	0.397
WASO	0.305	0.191
SFI	0.00	1.000
PSQI	-0.062	0.795
EES	0.035	0.882
Apnea	0.333	0.151
BMI	0.323	0.165

	Right (n = 8)	Left (n = 4)	Bilateral (n = 8)	P value
SE	64.10 ± 21.30	58.38 ± 27.63	75.45 ± 5.89	0.275
SL	23.50 ± 14.87	15.62 ± 14.99	15.44 ± 10.65	0.443
Arousal I	11.19 ± 7.81	26.12 ± 20.93	9.35 ± 6.58	0.222
RDI	16.00 ± 17.07	36.22 ± 48.62	19.92 ± 26.63	0.872
SPO_2	10.88 ± 19.42	3.25 ± 3.77	2.75 ± 3.33	0.967
WASO	61.88 ± 34.98	80.38 ± 50.79	41.75 ± 13.43	0.317
SFI	0.46 ± 0.26	0.50 ± 0.34	0.57 ± 0.22	0.466
PSQI	11.12 ± 1.89	13.00 ± 1.63	11.12 ± 1.81	0.223
ESS	11.62 ± 3.46	12.25 ± 2.06	11.62 ± 3.11	0.847

***Table 12**: Correlation between sleep parameters and types of diffuse white matter hyper-intensities, degree of brain atrophy and side of the lesion (Data are mean ± SD; n = 8 and 4; p > 0.05).*

Discussion

Sleep is considered to be important for cognitive function and cognitive deficits and moreover, sleep disorders are influenced by one another [20]. Given the rising prevalence of cerebrovascular diseases and dementia with aging, the development of more sensitive neuropsychological and neuroimaging diagnostic and prognostic tools will be critical for elucidating and modifying VCID pathophysiology to develop new modes of intervention for disease prevention and treatment, especially for the growing aging population.

The present study revealed significant correlation for Apnea, RDI and SPO_2 with BMI; more Apnea/H and RDI with high BMI and more average SpO_2 desaturation with high BMI. The results show that hypertension was present in 80% of VaD patients in this study. These findings denote the importance of hypertension as a risk factor for vascular dementia. This observation was supported closely by the report of Hebert., *et al.* [21]. In addition, hyperlipidemia and cardiac diseases were present in 80% and 60% of VaD patients, respectively. Diabetes was present in 50% of VaD patients in this study. The association between dementia and diabetes can be explained through the effect of diabetes cerebral blood flow especially with regards to reactivity and autoregulation or serving as a risk factor for clinically overt and silent brain insults.

In this study, the most common sleep complaints among VaD patients were EDS (65%), SDB (50%), insomnia (15%) and RLS and PLMS (15%) and RBD (5%), respectively. These results are in accordance with that of Ramirez-Santos., *et al.* [22] who stated that mild cognitive impairment and dementia, in general (regardless of type), are associated with a marked increase in sleep-related complaints. The global prevalence reported for any sleep disorder was 82%, with insomnia 37.1%, hypersomnia 47.8%, parasomnia 21.4% and apnea 54.5%. Similarly, Guarnieri., *et al.* [23] found that VaD patients had a higher frequency of sleep disturbances (insomnia, EDS, SBD, RBD and RLS) than that observed in AD patients. The highest risk increase with respect to AD was for SBD with the high frequency of OSA reported in stroke patients. Both the vascular damage and SDB have some common risk factors such as excessive BMI and hypertension [24].

In this study, there was a statistical significant correlation between CDR and MMSE and PSQI with the severe cognitive impairment and poor sleep quality which explain the high prevalence of SDB, insomnia, RLS and PLMS and RBD in VaD patients. Similar findings were reported by Mondal., *et al.* [25] who found that an abnormal ESS was more likely to have an abnormal PSQI score. But, the results of this study show no statistical significant correlation between CDR and MMSE and ESS, no relationship between grade of cognitive impairment and degree of excessive daytime sleepiness indicating that EDS can be found in the earliest stage of vascular dementia. Similar findings were reported by Miu and Szeto [26] found no correlation between MMSE and ESS among 105 of mild to moderate dementia patients. Furthermore, Merilino., *et al.* [27] showed that, although insomnia represented the most common sleep disturbance in 750 subjects aged 65 years or older, 86 of them were diagnosed as demented and this was not associated with cognitive impairment. However, the severity of SPO_2 desaturation was associated with high ESS and excessive daytime sleepiness. Those subjects with an abnormal ESS had higher BMI and higher AHI.

Taken together, the current data suggest that SE and continuity were poorer in patients with VaD in this study. The sleep-wake cycle is regulated by a complex interplay of mechanisms located mainly in the brainstem, hypothalamus and thalamus. Any lesion, such as an acute stroke, which can directly affect the thalamo-cortical network function, has the potential to disrupt the sleep-wake cycle and lead to sleep disturbances [28]. It is well known that lesions of the cortex might compromise this process with abnormal deactivation of frontal and thalamic areas from pre-sleep wakefulness to non-REM sleep and hence primarily affect sleep continuity [29].

In the present study, there was a significant negative correlation between AI and RDI and ADL and significant correlation for SE, AI and RDI with the ESS score severity. Similar results were reported by Jiang., *et al.* [8] as they found that patients with vascular cognitive impairment, no dementia had higher PSQI scores compared with controls. Compared with controls, patients had reduced TST, decreased SWS and REM sleep, longer SL, lower SE, and increased AI and PLMS index.

The present study was guided by the idea that REM sleep parameters may reflect different pathophysiological mechanisms between AD and VaD. It is now well established that cholinergic neurons are important determinants of REM sleep, with cholinergic activity low during SWS and high during REM sleep [30]. Stroke causes a central imbalance of neurotransmitters, such as acetylcholine, serotonin, and melatonin causing sleep structure abnormalities [31]. Similar REM parameter dysfunctions were present in AD with reduced REM duration and increased first REML episode [32]. However, this can be explained because of the dependence of REM sleep on the integrity of cholinergic neurotransmission and the widespread deterioration of cholinergic systems throughout the basal forebrain in AD [33].

The present study revealed a positive significant correlation between ESS, Apnea, RDI and SPO_2 and BMI score. Similar findings were reported by Bassetti., *et al.* [34], as they found a significant correlation between apnea–hypopnea index and BMI. In addition, Erkinjuntti., *et al* [35] reported that patients with MID tended to have more apneas/hypopneas than those with AD and apneas/hypopneas tended to increase in direct proportion to the severity of dementia. However, Karaca [36] found no correlation between BMI and sleep quality (PSQI). This discrepancy may result from differences in evaluation methods; subjective and/or PSG and differences in the patients' age range.

Circadian rhythm disturbances are common in patients with dementia and it can affect more than 80 % of those over age 65, resulting in insomnia, excessive daytime sleepiness and day/night reversal [37]. Similar to the present study, Guarnieri., *et al.* [23] found that VD patients had disrupted sleep-wake cycles associated with shorter sleep periods and lower sleep quality which were more significant than those in AD patients. Both the degradation of sleep quality and the disintegration of the sleep-wake cycle in VD may reflect the disruptive effects of the vascular lesions on the neural network dedicated to sleep regulation. The reason is that most of the lacunes in VaD are located predominately in the internal capsule, basal ganglia, and the periventricular white matter. These lesions could disconnect the pathways leading to and from the suprachiasmatic nucleus, which might be involved in the regulation of the circadian sleep-wake cycle. Furthermore, stroke lesions may alter other circadian functions such as sleep-related secretion of growth hormone and melatonin [38].

Post stroke hypersomnia or EDS is due to reduced arousal because of lesions involving the ascending arousal pathways. This occurs in patients with bilateral lesions of the thalamus, sub-thalamic and hypothalamic area, tegmental midbrain and pons where fibers of the ascending arousal pathways can be severely injured even by single small lesions [39]. WMH severity was significantly associated with sleep disturbance, with most symptoms related to daytime hyper-somnolence and restless sleep. This finding might be explained by disruption of the frontal-subcortical neuronal circuits and basal ganglia [40]. Baillet., *et al.* [41] found that a higher sleep fragmentation was associated with a reduction in white matter integrity due to white matter hyper-intensities (WMHs). Also, greater sleep fragmentation was associated with more severe arteriolosclerosis and subcortical infarcts in brain autopsies in community-dwelling older people [42].

Stroke-related insomnia are associated with caudate, subcortical, thalamic and brainstem (thalamo-mesencephalic, pontomes-encephalic, and pontine tegmentum) lesions. Patients may presented by inversion of the sleep-wake cycle with insomnia, night-time agitation and daytime hypersomnia [43].

Researchers have been unable to link SDB frequency, type, or severity to the location of the stroke. However, autonomic networks responsible for respiratory control may be disrupted with lesions in forebrain structures that control respiration as part of integrated behaviors such as speech or exercise (Sharma and Culebras 2016). Hemispheric strokes in the frontal cortex, basal ganglia or even internal capsule may cause respiratory apraxia, with impaired voluntary modulation of breathing amplitude and frequency, leaving patients unable to take a deep breath or hold the breath [44]. Also, the medulla may be less responsive to rising Pco_2 levels during sleep [45]. SDB, including OSA, central and mixed apnea, is linked with white matter disease on magnetic resonance imaging and silent strokes [46]. SDB patients are at a higher risk of developing cognitive impairment or incident of AD [47,48].

OSA is a common feature of vascular dementia leading to fragmented sleep, increased nocturnal confusion and excessive daytime sleepiness [49]. In the acute post-stroke period, there is a high prevalence of central apneas which is typically resolved [50]. Central sleep

apnea and Cheyne-Stokes respiration are caused by motor dysfunction leading to destabilization of the upper airways due to involvement of pyramidal-related musculature without affecting swallowing. This can also cause a higher instability of the upper respiratory tract during the night [51].

Post stroke PLMs may be of primary type. It is not always associated with sleep disturbance and may be due to unilateral hemispheric, pontine base or tegmentum and spinal strokes [52]. It is now well known that some patients with bilateral RLS have lesions in both the corona radiata and basal ganglia, whereas other patients have lesions only in the corona radiata with either contralateral or bilateral RLS [53]. Most commonly, RLS was accompanied by PLMS in sleep [42]. A common mechanism behind both PLM and RLS might be due to dysfunction of the dopaminergic system, possibly on the level of either pre- and/or post-synaptic striatal and/or spinal dopamine receptors [54]. There is evidence to support an association between wandering in dementia and RLS and/or PLMS. Moreover, neuroimaging studies have suggested reduced dopamine reuptake in the caudate and putamen among AD patients who wander relative to those who did not [55].

Cases of stroke have been described in association with RBD. These include lesions in the pontine tegmentum, midbrain, or paramedical thalamus which may trigger visual hallucinations, especially at sleep onset [56]. Strokes at thalamus, temporal, parietal, and occipital lobes may lead to increased dreaming and nightmares and/or a syndrome of dream-reality confusion [57]. Patients with strokes in the pons, midbrain, or paramedian thalamus may experience peduncular hallucinosis which characterized by complex, colorful, dreamlike visual hallucinations, especially in the evening and at sleep onset. Peduncular hallucinosis may represent a release of REM sleep mentation and may be associated with insomnia [43].

In this study, there were no significant correlation between MRI findings (the presence of cortical vs subcortical infarction, frontal, thalamic or lacunar infarction, different types of diffuse white matter hyper-intensities, degree of brain atrophy and side of infarction; left, right or bilateral) and sleep parameters (subjective sleep assessment; ESS and PSQI or PSG parameters; SE, SL, AI, RDI and SPO_2, WASO and SFI). This might be due to associated widespread injury and dysfunction throughout the brain in cases of stroke [58]. Similar findings were reported by Karaca [34] who reported that there was no significant correlation between right–left cerebral involvement and sleep quality. Lutsey., *et al.* [59] found that neither OSA nor abnormal sleep duration was statistically significantly associated with cerebral infarcts, WMH brain volumes or regional brain volumes by MRI imaging in VaD and AD patients.

However, some studies suggest that right-sided strokes decrease REM and REM density, while left-sided strokes decrease NREM stages. Körner., *et al.* [60] found that slow-wave sleep was decreased in infarctions of the left hemisphere stroke patients. While Pasic., *et al.* [61] and Da Rocha., *et al.* [62] reported that the involvement of the right cerebral hemisphere is more frequent in patients with post stroke sleep disorder, insomnia, fragmented sleep, difficulty in falling asleep, greater sleep latency and worse subjective sleep quality Similarly, Wu., *et al.* [63] found that patients with minor thalamic lesions are at increased risk for sleep disturbance, sleep-related breathing disorders, and memory deficits. In this respect, the results are contradictory, and further studies with large number are needed.

The available data confirm that sleep is significantly impaired in patients with VaD at both subjective level and the objective by PSG recordings which may be used as a surrogate marker of vascular dementia**.** Much evidence suggests that daytime sleepiness, sleep disturbances or SBD are associated with an increased risk for vascular dementia, ischemic stroke, hypertension, and heart disease [64]. Since sleep disorders are frequent and can have serious consequences on patient's health and quality of life and some sleep disorders are more challenging to treat, it is the consensus that most can be easily managed with adequate interventions.

Simple questions of the patient or bed-partner for the symptoms and signs of the OSA, such as loud snoring, observed apneas, and daytime sleepiness, would help to identify those in need of further diagnostic evaluation as OSA is a treatable disorder [65]. A careful clinical evaluation of sleep disorders should be performed routinely in the clinical setting of persons with cognitive decline. Instrumental assessment; PSG should be used in selected patients.

Limitations and Strengths

This study has some limitations which have to be taken into consideration. First, the sample size was relatively small, resulting in low statistical power for detecting significant differences between groups. Second, there were difficulties in doing second PSG to confirm results and any day to day variation of sleep disturbances. Third, the sample lack different stages of VaD, as severe cases were excluded from the study.

Despite these limitations, this work is unique in that:

a) It used an extensive clinical evaluation including a combination of neurological examinations and detailed neuropsychological tests in order to define the cognitive status of each participant.

b) It undertook assessment of sleep disorders by means of subjective and objective instruments such as PSG which is essential for a correct diagnosis of some sleep disturbances including SDB which measures sleep architecture.

c) The study employed state-of-the-art brain MRI to assess the patients.

d) The study provided insights into sleep disturbances in VaD patients and highlights the importance of this frequently missed aspect in the care of dementia patients and their caregivers.

Conclusion

It is concluded that the information provided in this study can help to provide insights into the importance of sleep disturbance in vascular dementia patients and highlights the importance of this frequently missed aspect in the care of dementia patients and their caregivers. Sleep disorders can be detected in early stages of VaD**.** The most common sleep complaints among VaD patients were EDS, SDB, insomnia and RLS and PLMS and RBD, respectively. The more severe the cognitive impairment (MMSE and CDR), the poorer is the sleep quality (PSQI). This in turn can explain the high prevalence of SDB, insomnia, RLS and PLMS and REM behavioral disordered in VaD patients.

PSG study of VaD patients showed poorer SE, prolonged SL and high AI. In addition, VaD patients spend more time in stage I, less time in SWS and REM sleep, together with delayed REML and less 1st REML. In addition, PSG findings increased sleep fragmentation (more WASO and SFI), increased AI and PLMS index. VaD patients had significant high Apnea, Hypopnea and RDI score with high average SPO_2 desaturation. Early detection and treatment of SBD in these cases may be of utmost importance and may prevent further cognitive decline.

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